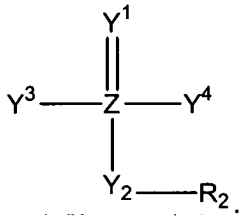
REMARKS

Claims 1-102 have been cancelled without prejudice to continued prosecution. New claims 103-136 have been added to contrast agents (claims 103-118), metal chelating ligands (claims 119-134), and pharmaceutical compositions (claims 135-136). Support for new claims 103-136 can be found throughout the specification, including, for example, at page 13, lines 5-7, page 15, lines 6-8, page 27, line 26, page 28, lines 5-13, page 30, page 31, lines 14-16, page 38, page 50, and original claims 61, 77, 83, and 84.

The specification has been amended to incorporate the priority information recited in the transmittal letter filed with the present application on December 20, 2001.

Applicants note that two different structures in the specification (e.g., compare structures at page 29 and page 30 of the specification) contained "R_2" moieties. For clarity, Applicants have amended the specification to replace "**R_2**" with -- **R_2'** -- in the following structure:



Applicants also have replaced page 38 of the specification with a substitute page 38. Due to a photocopying error, the structures on the lower portion of page 38 were not identified. In substitute page 38, the lower two structures have been identified as MS-327 and MS-328 (see original claims 75 and 82).

No new matter has been introduced by the above amendments. Applicants ask that claims 103-136 be examined.

No extra claim fees are due. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

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Version with markings to show changes made

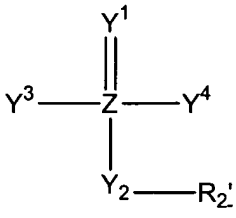
In the specification:

Paragraph beginning at page 18, line 20 has been amended as follows:

Examples of chemical groups which would serve as a BHEM include carbon, phosphorous, tungsten, molybdenum, or sulfur atoms having attached charged or neutral heteroatoms such as oxygen, nitrogen, sulfur or halogens (especially fluorine) possessing two or more lone electron pairs (i.e., full or partial negative charge) or electropositive hydrogen atoms (i.e., protonated amine) for hydrogen bonding with water. These include groups such as sulfone, ether, urea, thio-urea, amine, sulfonamide, carbamate, peptide, ester, carbonate and acetals. Preferred groups include those which possess one or more partial or full negative charges in aqueous solution at physiological pH wherein the negatively charged atoms cannot be partially or fully neutralized by covalent or coordinate covalent bonding to the IEM. Examples of these preferred BHEMs include negatively charged groups such as phosphate mono-ester, phosphate diester, carboxylate, and sulphonate. More preferred are those which have phosphate groups or any ester forms thereof. Even more preferred are phosphate diesters, since: a) they are highly hydrophilic with four hydrogen-bonding oxygens; b) they are relatively readily synthesized using techniques shown below; c) they serve as excellent linkers between the IEM and the PPBM; and d) because phosphate compounds exist and are metabolized naturally in the body, phosphate diester-containing contrast agents are expected to be non-toxic.

Paragraph beginning at page 28, line 14 has been amended as follows:

If the moieties of this invention are positioned in the contrast agent as in structure (1) above, the BHEM is preferably sulfone, urea, thio-urea, amine, sulfonamide, carbamate, peptide, ester, carbonate, acetals and more preferably



or ester forms,

where Z = P, W, Mo, or S

Y^1, Y^2 = O or S

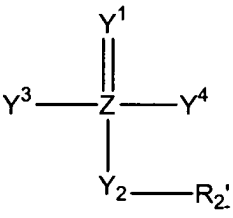
Y^3, Y^4 = O, S or not present

R_2' = H, C_{1-6} alkyl or not present.

Most preferably, the BHEM is a phosphate group.

Paragraph beginning at page 28, line 37 has been amended as follows:

If the moieties of this invention are positioned in the contrast agent as in structure (2) above, the BHEM is preferably sulfone, urea, thio-urea, amine, sulfonamide, carbamate, peptide, ester, carbonate, acetals and more preferably the BHEM has the following formula:



or ester forms,

where Z = P, W, or Mo

Y^1, Y^2 = O or S

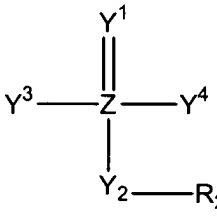
Y^3, Y^4 = O, S or not present

R_2' = H, C_{1-6} alkyl or not present.

Most preferably, the BHEM is a phosphate group.

Paragraph beginning at page 29, line 19 has been amended as follows:

If the moieties of this invention are positioned in the contrast agent as in structure (3) above, the BHEM is preferably SO_3^- or ester forms, sulfone, urea, thio-urea, amine, [sulfonamie] sulfonamide, carbamate, peptide, ester, carbonate, acetal and more preferably



or ester forms,

where Z = P, W, Mo, or S

Y^1, Y^2 = O or S

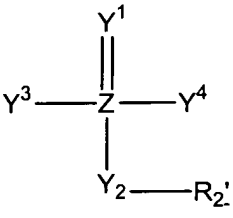
Y^3, Y^4 = O, S or not present

R_2' = H, C_{1-6} alkyl or not present.

Most preferably, the BHEM is a phosphate group.

Paragraph beginning at page 31, line 14 has been amended as follows:

For contrast agents comprising the formulas shown above, the metal ion M is more preferably Gd(III), Fe(III), Mn(II), Mn(III), Cr(III), Cu(III), Dy(III), Tb(III), Ho(III), Er(III) or Eu(III), and most preferably Gd(III). The BHEM is preferably sulfone, ether, urea, thio-urea, amine, amide, [sulfonamie] sulfonamide, carbamate, peptide, ester, carbonate, acetal and more preferably COO^- or ester forms, SO_3^- or ester forms and



or ester forms,

where Z = P, W, Mo, or S

Y^1, Y^2 = O or S

Y^3, Y^4 = O, S or not present

R_2' = H, C_{1-6} alkyl or not present.

In the claims:

Claims 1-102 have been cancelled.